

### REMARKS

Reconsideration and withdrawal of the rejections of the claims, in view of the remarks and amendments herein, is respectfully requested. Claims 1 and 8 are amended, claims 7, 28-35, 49-66, 70, 72, and 74 are canceled, and claims 75-88 are added. Claims 1-6, 8-27, 36-48, 67-69, 71, 73, and 75-88 are pending in this application.

Applicant submitted a Supplemental Information Disclosure Statement and a 1449 Form on March 19, 2008. Applicant is enclosing a copy of the previously submitted 1449 Form which includes the reference the Examiner did not initial. Applicant respectfully requests that an initialed copy of the 1449 Form be returned to Applicant's Representatives to indicate that the cited reference has been considered by the Examiner.

#### *The 35 U.S.C. § 112, Second Paragraph, Rejections*

Claims 1-12 and 68-74 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The amendment to claim 1 to delete "capable" and the amendments to claim 8 obviate the rejections thereto. Accordingly, withdrawal of the § 112(2) rejections are respectfully requested.

#### *The 35 U.S.C. § 103 Rejections*

Claims 1-3, 5, 9, and 68-69 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Dunn et al. (U.S. Patent No 6,248,569) in view of Thach (U.S. Patent No. 5,342,782). Claims 1-12 and 68-74 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Dunn et al., Thach and further in view of Kappelman et al. (Gene, 160:55 (1995)) and the results of a search in the New England Biolab catalog for "3'" and "AT" overhang. These rejections are respectfully traversed.

The Examiner asserts that Figure 2 in Dunn et al. teaches a vector comprising a site for a first restriction site that generates a 3' TA overhang (i.e., *PacI*) which is 5' to a site for a second restriction enzyme which generates blunt ends (i.e., *HpaI*), and a promoter positioned 5' of the first site, such that DNA comprising an open reading frame inserted between the first and second site would have a 1 in three chance of being in frame with the open reading frame upstream of the first restriction site. The Examiner also asserts that Figures 1A-B in Dunn et al. disclose a

vector comprising a first site for *PacI*, with sites for blunt cutters such as *ScaI* and *NruI* 3' of said site, with a promoter positioned 5' to the first site.

Dunn et al. generally relate to methods for the introduction of unidirectional deletions. The vectors in Figures 1A-B, pND-1 and pND-2, respectively, are employed to clone DNA (see column 5, lines 30-41). A fl origin is 5' to the *PacI* site in pND-1 and repL (a *Pi* lytic replicon; 5' to 3') is 5' to the *PacI* site in pND-2. pZIP in Figure 2 is disclosed as useful for cloning normalized full-length cDNA libraries and for generating nested deletions (column 8, lines 8-11). Both pND-2 and pZIP have a fl origin, a site at which a single strand nick is produced by a fl protein. That nick allows unidirectional exonuclease III digestion.

The vectors in Figures 1A-B of Dunn et al. do not include an apparent promoter 5' to a recognition site for a restriction enzyme that generates a 3' TA overhang. pZIP does not include a promoter that is 5' to a recognition site for *SgfI* which is 5' to a recognition site for a second restriction enzyme. Nor does pZIP include a promoter that is 5' to a recognition site for a restriction enzyme that generates a 3' TA overhang, which is 5' to a recognition site for one of *PmeI*, *EcoRV*, *BalI*, *DraI*, *HincII*, *SciI*, *SwaI*, *BsaBI*, *EcoICRI*, *Hpy8I*, *MlyI*, *MslI*, *PshAI*, *SspD5I*, or *XmnI*, which in turn is 5' to a selectable marker gene and sequences for replication and/or maintenance of the vector.

The Examiner asserts that column 4, lines 36-64, of Thach teaches that one may adjust the sequence of an open reading frame such that it is in-frame with an upstream promoter.

There is no "reading frame" for a promoter so that a downstream sequence is transcribed. Moreover, column 4, lines 36-64, of Thach does not relate to directional cloning.

With regard to Dunn et al. and Thach, the Examiner alleges that it would have been obvious to one of ordinary skill in the art to have altered any out of frame sequence inserted in the vector of Dunn et al., in order to obtain the correct reading frame, as taught by Thach.

Dunn et al. and Thach, individually or in combination with each other, do not provide a reasonable expectation for a directional cloning and expression vector having the capability of expressing introduced open reading frames without fusion to upstream coding sequences or as a fusion by employing a restriction endonuclease that yields a 3' TA overhang.

Kappelman et al. (although cited as a reference against the claims, this document was not specifically mentioned in support of the reasoning for rejecting the claims) disclose the isolation

of the restriction endonuclease *SgfI*, which yields a 3' TA overhang after cleaving double stranded DNA having a recognition site for *SgfI*.

The search results from the New England Biolab catalog (although cited as a reference against the claims, this document was not specifically mentioned in support of the reasoning for rejecting the claims) provide a list of restriction endonucleases that yield a 3' TA overhang after cleaving double stranded DNA having a recognition site therefor.

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to have inserted a well known site such as *SgfI* in the vector of Dunn et al. in view of Thach, since the use of any particular restriction enzyme site in a vector is well known in the art, and since the placement of known and useful restriction sites, such as *SgfI*, in any vector, for manipulation of DNA, was extremely well known in the art. The Examiner concludes that based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

None of the cited documents, individually or in combination, provide a reasonable expectation of a vector capable to expressing an introduced open reading frame without or with a N-terminal fusion, where the vector has a site for a restriction enzyme that generates a 3' TA overhang, useful to form an exchange site at the 3' end of a vector backbone and 5' end of a DNA to be inserted. The use of blunt ends forming an exchange site at the 5' end of a vector backbone and the 3' end of a DNA to be inserted allows for termination of a coding region in the DNA insert near the exchange site. And the use of both 3' TA overhangs and blunt ends allows for combinations of the above.

Therefore, withdrawal of the § 103 rejections is respectfully requested.

**CONCLUSION**

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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Date

December 5, 2008

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 5th day of December, 2008.

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Cheryl Dankers